DEPARTMENT OF

PHYSIOLOGY AND PHARMACOLOGY

ANNUAL REPORT

2013 - 2014

1. EXECUTIVE SUMMARY FOR 2013-2014

This was a successful year for the department, with substantial accomplishments in education, research productivity, and service to the institution and to the scientific community.

With the outstanding dedication, effort, expertise and enthusiasm of our teachers, we were able to maintain our history of educational excellence and leadership. The faculty provided significant teaching in several programs, and also directed many courses, including courses in the M.D. curriculum, Physician Assistant Studies, MSBS program for students seeking entry to medical school, and graduate studies in Biomedical Sciences. The outcomes, as shown by examination results and by student ratings of our efforts, have been quite positive. Standardized examinations, such as the USMLE step-1 exam and the Physician Assistant National Certifying Exam, support the assessment that we have done a good job. Our largest contribution to the M.D. program is in the Organ Systems course. This year, Dr. Beavis was course director, and did an outstanding job. Dr. Nitin Puri served as assistant course director. Many faculty participated in our educational efforts, as shown below, but it is worth noting that Drs. Beavis and Puri once again provided a large portion of the Pharmacology and Physiology teaching to our medical students, as well as to other degree students.

Our department faculty and students were productive in their research activities. This is reflected in the number of papers published, grant funding, and presentations locally and at national and international meetings. However, with the loss of faculty, we are smaller and have had some decreases in the number of publications and in the amount of extramural funds as compared to recent years. Even so, our faculty and students were responsible for over 3.7 million dollars in research expenditures from our extramural funding. Closely related to our successful research programs, six graduate students defended their Ph.D. dissertations during the past year.

The faculty provided a significant level of institutional service, serving on numerous college and university committees. In addition, we served the scientific community as reviewers for many manuscripts, served as members of editorial boards, served on expert review panels for research grant proposals, and served as session chairs at scientific meetings and otherwise provided service to professional societies.

The biggest threat to our progress was in the form of a truncated and poorly-conceived chair search that was not completed due in part to a delayed start in the face of the impending departure of our former dean. Unfortunately, much of the discussion seemed driven by perceived problems rather than the documented strengths of our department and the successes of our faculty and students. This was a great distraction that affected all members of our department and likely did some harm. In spite of this, the faculty, students and staff continued to work diligently and professionally, and we have continued to be a leading department in research and education within the College of Medicine and Life Sciences. With a new administration in place, we are looking forward to a proper search for a new chair for our department.

Goals for 2014-2015. Last year, this section spoke of the chair search and stated that a major goal was to "focus on our work; it is not a time to pause to wait and see what happens". As we look forward to a proper chair search this year, this goal remains applicable.

A top priority for this year must be to actively assist in a new search for a chair, providing the Dean and the search committee with whatever ideas, time and effort we can. It is crucial that we all put our best foot forward, emphasizing our many strengths, and working together toward our common goals. We must also put aside any residual concerns that might be left from the last search. Such feelings are not useful and can only serve to distract from the important work that needs to be done.

A goal every year is to provide extramural support for our research programs. The recent decline is attributable to the loss of faculty, most recently Drs. Abraham and Xie. Other than them, our core research strength remains intact. It is worth noting that those who have active research programs, both funded and currently unfunded, have been working hard to secure continued and additional support, and I am confident that these efforts will continue, and not be in vain. Two important developments already bode well for next year. These are the successful grant application, submitted by Dr. Kumar, that will be funded soon, and the pending receipt of a K01 Faculty Development Award to Dr. Hinds. I am optimistic that the chair search will produce a well-funded scientist prepared to lead the department, including recruitment of additional faculty to maintain and expand our research.

Regarding our teaching programs, in addition to our current teaching activities, the chair and course directors will work with chairs and course directors from other departments to help ensure that the UTCOM educational programs remain first-rate even as some senior faculty retire.

2. CHAIR'S SELF ASSESSMENT

Interim Chair of the Department: Though I did not seek this position, I accepted Dr. Gold's request in late 2012 to take over while a search process could take place. Though my appointment was not effective until Feb. 1, 2013, Dr. Abraham's absences meant that I was *de-facto* chair most of the time from mid-November, 2012. After the failed search and the virtual simultaneous departure of Dr. Gold, the interim Dean, Dr. McGinnis, asked me to remain as Interim Chair, and I agreed. The unfortunate search added to the strain on our faculty and to a sense of concern over the future. During these times, I have attempted to provide stability, support and guidance in an effort to sustain the department's productivity in research and in teaching, and I believe that this was accomplished. I have also tried to provide guidance to some junior faculty, with the welcome and invaluable help of our senior colleagues. Though resources are limited, I do feel that I have been able to provide a period during which our faculty could focus on their academic lives with as few distractions as possible.

Teaching in the M.D. Program. In the Organ Systems Block for the second year medical students, I continued providing many hours of teaching, and received positive feedback. I also spent time working with individual students, and helping the course director as needed. I also continued service on two curriculum committees related to our M.D. program.

Teaching PA students was an important part of my efforts. Student feedback and exam results indicate that I did a good job.

Committee Service responsibilities were a significant use of my time. In addition to the other committees, many hours were spent as a member of a committee for the LCME self-study. I also was heavily involved before and during the site visit in my roles as chair, member of the Executive Curriculum Committee, and member of the Pre-clinical Curriculum Committee.

2014-2015 Goals:

I will continue to provide whatever support I can to the faculty, students and staff so that we remain productive. I will help the Dean and the chair search committee in whatever way I can to move toward a successful outcome of the upcoming search process.

I will work with course directors and others to help identify faculty to take over my teaching in future years.

Once a new chair is in place, I will remain available to provide assistance, if asked, during the transition.

3. DEPARTMENT HIGHLIGHTS & NOTABLE EVENTS

Six doctoral students: **Moumita Banerjee, Qiming Duan, Xingjian Jin, Varunkumar Pandey, Moustafa Sayed**, and **Jian Wu** successfully defended their dissertations, completing the work for their Ph.D. degrees.

Latrice Faulkner, a doctoral student working with **Dr. Jennifer Hill**, received several awards to support her studies: **(1)** the National Institute of General Medical Sciences (NIGMS) Ancillary Training Program Scholarship to attend the Keystone Symposium meeting on "Obesity: A Multisystems Perspective", Vancouver, British Columbia, Canada, 2014. **(2)** an individual NIH Ruth L. Kirschstein National Research Service Award to Promote Diversity in Health-Related Research, and **(3)** a NIH Summer Student Intramural Research Training Award (IRTA) Fellowship through NICHD.

Drs. Kathirvel Gopalakrishnan, Meenakshi Kaw, Sivarajan Kumarasamy and Brahma Raju Mopidevi were appointed as Assistant Professors in the Research Track.

Dr. Kathirvel Gopalakrishnan, was selected for oral presentation at the 2013 International Meeting – Rat Genomics and Models, Cold Spring Harbor Laboratory, NY.

Dr. Jennifer Hill, Assistant Professor received the Michigan Diabetes Research Pilot & Feasibility Study Grant, January 2014

Dr. Terry Hinds has been named to the Editorial Board of the Journal of Diabetes Research.

Dr. Bina Joe, Professor and Director, Center for Hypertension and Personalized Medicine has been named the 2014 Lewis K. Dahl Memorial Lecturer by The American Heart Association's Council on High Blood Pressure Research. She presented this lecture at the conference in San Francisco, CA, September, 2014. **Dr. Joe** also received the 2014 Distinguished Service Award, American Physiological Society, Physiological Genomics Group.

Dr. Sivarajan Kumarasamy was elected for oral presentation at the 2013 International Meeting – Rat Genomics and Models, Cold Spring Harbor Laboratory, NY

Dr. Beata Lecka-Czernik, was recognized through press releases and commentaries on her research described in Rocket Science.

Dr. Brahma Raju Mopidevi, Assistant Professor was awarded a Kidney Council New Investigator Travel Award for the abstract he submitted "A Genetic Variant of Human Aldosterone Synthase Gene Causes Salt-Dependent High Blood Pressure in Transgenic Mice". This will be presented at The High Blood Pressure Research Meeting in Hilton San Francisco, September, 2014.

Dr. Sonia M. Najjar, Professor and Director of CeDER, was honored by being named the Frederick W. Hiss Endowed Professor in Diabetes Research. **Dr. Najjar** was also honored by being named a recipient of the YMCA Milestone Award, honoring women who have been making a difference in Northwest Ohio. **Dr. Najjar** also organized last year's International Symposium for CEA. This important international scientific congress brought together scientists from across the country and around the world right here in Northwest Ohio.

Resmi Pillai, doctoral student working with **Dr. Bina Joe**, won the Young Investigator Award from the American Physiological Society (APS), which is awarded to the first author of the best paper published in an APS journal-*Physiological Genomics* in 2013.

Alisha Sangal, Summer Surf Student working with **Dr. Jennifer Hill**, received the USRCAP Research Fellowship, Summer 2014.

Dr. Lance Stechschulte, a postdoctoral fellow in **Dr. Beata Lecka-Czernik's** laboratory, received multiple awards for his work that will be presented at the meeting of the American Society for Bone and Mineral Research, Houston, TX in September. One abstract will be featured 4 times in the form of oral presentation, plenary poster, during a guided poster tour, and during a special symposia on Bone and Diabetes. A second abstract will be presented orally and is the basis for Dr. Stechschulte being awarded a Young Investigator Travel Award.

Dr. John W. Turner, Jr., was the recipient of the 2013 UTCOM Career Research Award.

Harshal Waghulde, doctoral student working with **Dr. Bina Joe** had his research recognized several times: (1) the work was selected for an oral presentation at the 2013 International Meeting – Rat Genomics and Models, Cold Spring Harbor Laboratory, NY; (2) his work was selected for an oral presentation at the 2013 American Physiological Society – Experimental Biology meeting held in San Diego, CA; and (3) He won a research award for his research presentation at the Experimental Biology meeting 2013.

Dr. Zi-Jian Xie departed University of Toledo January 1, 2014. Dr. Xie is now the founding Director for Interdisciplinary Research at Marshall University, Huntington, WV.

4. DETAILS OF EDUCATION, RESEARCH, AND ADMINISTRATIVE & UNIVERSITY SERVICES

4a. EDUCATION

The department faculty were actively engaged teaching students in multiple programs. Percent efforts are presented in the table shown below. In the M.D. program, our main responsibility was running the Organ Systems Block in the second year (course director, Dr. Beavis), and providing a substantial portion of the content. Organ Systems runs from mid-August to about the end of April each year, provides approximately half the contact hours for the sophomore year of our M.D. program, and involves faculty from our department, the Pathology Department, and several other departments. With primary responsibility for this block, the course director and our office staff provide a substantial effort over much of the year. We also teach several topics in the Immunity and Infection block, and cover the genetics content in the Cell and Molecular Biology Block. Another important responsibility is teaching the Fundamentals of Pharmacology course for students in the Physician Assistant (PA) Studies Program (course director, Dr. Beavis). Also of note, Dr. Cicila is course director for Advanced Human Physiology for students in the MSBS program, for the Human Physiology course for our PA students, and for the Basic Genetics course for the PA students. Dr. Beavis directs the Pharmacology unit of the "Scientific Foundations" course in the Human Donations Science program.

The department is also home to the Cardiovascular and Metabolic Diseases [CVMD] track in the biomedical sciences graduate program (Track Director, Dr. Beavis). During the past year CVMD students studying with Physiology & Pharmacology faculty presented several oral or poster abstracts locally and at national or international meetings and were authors on several publications; these are included below in the lists of abstracts and published papers. Six students studying with our department faculty successfully completed the requirements for their Ph.D. dissertations. The Physiology and Pharmacology faculty teach core courses for the CVMD track, including Advanced Topics in CVMD (Dr. Puri, course director) and the seminar course (Dr. Vazquez, course director). We teach the Systems Pathophysiology course, which is directed by Dr. Lecka-Czernik who has a joint appointment in the department. Other important courses in the overall biomedical sciences graduate program are directed by Dr. Joe (Grants Writing Workshop) and Dr. Sanchez (Cell Biology and Signaling). Dr. Modyanov teaches the graduate course in Protein Structure and Catalysis.

Reviewing our faculty teaching, it can be seen that we are heavily involved in teaching students in multiple programs and, as noted above, have provided significant service in our roles as course directors. Other educational leadership is shown by our service on various education committees in the College of Medicine and in the Graduate School, listed in in Section 4.d., Administrative and University Services.

4b. RESEARCH

The department had success in our research endeavors, as noted by our many publications and by extramural funding, and by the recognition of the scientific community when we receive invitations to serve as peer reviewers for research grant proposals and manuscripts, and requests to present research findings and to chair sessions at scientific conferences. The following sections provide the details.

Faculty Effort for Research is included in the table below**.**
Effort for each technical staff and postdoctoral fellow was 100% for research.

Faculty Effort for Research, Teaching and Service.

NAME	TEACHING	RESEARCH	SERVICE
Andrew Beavis, Ph.D.	40%		60%
George T. Cicila, Ph.D.	50%	20%	30%
Kathirvel Gopalakrishnan, Ph.D.		100%	
Jennifer Hill, Ph.D.	20%	65%	15%
Terry Hinds, Ph.D.	20%	70%	10%
Sudhir Jain, Ph.D.		100%	
Bina Joe, Ph.D.	5%	65%	30%
Meenakshi Kaw, Ph.D.		100%	
Ashok Kumar, Ph.D.	5%	90%	5%
Sivarajan Kumarasamy, Ph.D.		100%	
Nikolai Modyanov, Ph.D.	35%	35%	30%
Brahma Raju Mopidevi, Ph.D.		100%	
Sonia Najjar, Ph.D.	5%	65%	30%
Nitin Puri, M.D., Ph.D.	70%	20%	10%
Phillip T. Robinson, D.V.M., MS			100%
Howard C. Rosenberg, M.D., Ph.D.	40%		60%
Edwin Sanchez, Ph.D.	25%	55%	20%
John W. Turner, Jr., Ph.D.	5%	85%	10%
Guillermo Vazquez, Ph.D.	17%	73%	10%

Space: All space for Physiology & Pharmacology is accounted for in the table below.

1st FLOOR BHSB - CEDER

Room Number	Room Use	Square Feet
141	Lab	1,623
142	Lab	1,575
142A	Office	138
142B	Office	162
144	Lab	323
145	Lab	205
146	Lab	234
147	Lab	189

2nd FLOOR BHSB

Room Number	Room Use	Square Feet
202	Lab	653
203	Lab	648
204	Lab	642
206	Office	153
213	Office	154
214	Office	153
217	Dark Room	78
222	Lab	504
223	File Room	92
226	Lab	120
226A	Lab	100
227	Lab	255
228	File Room	157
231	Lab	268
233	Lab	635
234	Shared Room	130
237	Office	161
237A	Office	302
237B	Office	170
238	Lab	355
238A	Lab	502
239	Lab	320
239B	Lab	431
240	Lab	422
242	Office	154

244	Office	154
246	Office	156
247	Office	159
248	Office	156
249	Office	92
251	Lab	180
253	Lab	50
254	Lab	143
255	Lab	267
255A	Lab	213
255B	Lab	119
255C	Lab	138
256	Lab	153
257	Lab	184
259	Lab	259
262	Lab	264
263	Lab	253
265	Lab	643
266	Lab	648
267	Lab	652
268	Office	68
269	Office	113
270	Office	105
271	Office	106
275	Common Area	362
276	Storage Room	79
277	Office	138
278	Office	130
282	Office	763
283	Office	126
284	Office	271
285	Office	110
286	Office	119
287	Office	120
288	Office	98
289	Conference Room	317

3RD FLOOR BHSB

307	Lab	132
308	Office	154
310	Office	154
312	Office	157
313	Office	157
315	Shared Room	112
317	Shared Room	78
319	Office	103
320	Office	99
321	Xerox Room	77
329	Lab	160
331	Shared Room	255
336	Lab	859
337	Lab	319
338	Lab	867
339	Lab	647
341	Lab	593
341A	Office	121
341B	Lab	142
342	Shared Room	121
343	Lab	767
343A	Lab	90
343B	Office	192
346	Office	208
348	Office	101
349	Office	156
351	Office	313
362	Shared Room	249
364	Lab	210
366	Lab	158
368	Lab	154
368A	Lab	152
369	Lab	641
375A	Conference Room	375
375B	Conference Room	327
376	Common Area	99
378	Office	130
381	Office	190
382	Office	125
383	Office	125

384	Office	125
385	Office	125
386	Office	134
387	Office	154

Funding: The Department's extramural research funds are included in the information shown in Table 3, provided by our Research and Sponsored Programs Office.

Grants Accounting provided "expenditures" for FY14 and the 4 years prior. These data are as shown in the table below:

Dept. of Physiology & Pharmacology Grant Expenditures

Fiscal Year	Expenditures
2010	$ 3,425,519
2011	$ 4,552,541
2012	$ 5,553,815
2013	$ 5,157,045
2014	$ 3,730,999

Brief Description of department research programs: The research programs for each of the faculty are described below. We have two centers within the department, the Center for Diabetes and Endocrine Research, and the Center for Hypertension and Personalized Medicine. The presence of these centers is the result of the forward thinking and enthusiasm for science of the directors. Many of our department faculty are members of one or both of these centers, as are faculty from other departments and colleges. These provide a focus for collaborative work, sharing of ideas, and graduate education. The names of the centers also provide an overview of the thrust of much of our work, though we also have other significant areas of work, including signaling mechanisms related to the biomarkers of stress, immuno-contraception, vascular mechanisms of atherosclerosis, hypothalamic mechanisms related to obesity and fertility, and others. These are described in the next paragraphs.

Kathirvel Gopalakrishnan, Ph.D., Assistant Professor – Dr. Gopalakrishnan's current research is focused on understanding the genetic components of pathophysiological conditions of the cardiovascular, renal complications. The most prominent of all complex traits investigated in our laboratory is blood pressure regulation using hypertensive rat models. Understanding the genetics of hypertension in humans is complicated by a number of genetic and non-genetic confounding factors. Rat models serve as valuable alternatives to human studies for the identification and characterization of genetic factors/genes. The main strategy is to identify the disease causative genetic factor/gene based on its location on the rat genome by linkage analysis and substitution mapping. BP QTLs (blood pressure quantitative trait loci) are genetic elements that causally contribute to the development of high BP. Using the

congenic approach; we have generated several congenic strains and mapped BP QTLs to various resolutions on rat chromosome 1, 9 and 10. The highest resolutions of mapping ranges from <805kb, <81kb and <42.5Kb. The interesting aspects of these important studies are that 1) they contain novel genes *Adamts16* (A Disintegrin-like metalloproteinase with thrombospondin motifs-16), *Rffl* (Rififylin) and Long non coding RNAs (LncRNAs) previously not known to function in BP control; and 2) These novel genes are homologous to human genes associated with BP control. We have successfully created the genetically-engineered rat *Adamts16* gene knockout rat model using zinc-finger nucleases (ZFN) and this model is very valuable tool for further mechanistic studies. Dr. Gopalakrishnan's primary research is utilizing this rat knockout model to determine the functional significance of *Adamts16*, from our congenic analyses with respect to blood pressure regulation. Very recently I have initiated the investigation of the genetic and molecular role of long non coding RNAs (LncRNAs) with respect to cardio vascular disease. The results from the next generation RNA sequencing (NGS) and LncRNA microarray on the hypertensive rats strains (Dahl S, R and SHR rats) revealed several differentially expressed LncRNA candidates (*Asb3, Chac2, Pex11b, Sp5, Scand1* and *Bcl6*) related to cardiovascular disease and those candidates are also have association in human GWAS studies related to cardiovascular disease. We have fine mapped 42.5 Kb QTL region on rat chromosome 10 and this region contains one gene Rififylin (*Rffl*) and up-regulation of *Rffl* is linked to hypertension, cardiac hypertrophy and Short QT interval and delayed endocytic recycling within cardiomyocytes in the S.LEW congenic rat compared to the Dahl S rat. The mechanism mediating up-regulation of *Rffl* is unknown. Recently I have identified that the critical genomic region of 42.5kb contains two novel long non coding RNA (LncRNA) SNRRL1&2 using the next generation RNA sequencing. Both are predicted to be targeting *Rffl* gene and DNA sequencing of the critical region revealed polymorphisms within the LncRNAs. The overall hypothesis is that the impaired action of novel long non-coding RNA molecule/s resulting in altered protein expression of rififylin is mechanistically linked to the development of hypertension. Dr. Gopalakrishnan's future goal will be investigating functional mechanisms of these several candidates with respect to cardiovascular disease. The expectation is to be able to translate my observations in rat models to disease causative mechanisms in humans and try to develop LncRNA biomarkers for cardiovascular disease.

Jennifer Hill, Ph.D., Assistant Professor – Dr. Hill's laboratory's interests lie in understanding hypothalamic homeostatic mechanisms controlling body weight and fertility and the interactions between these two systems. The brain blocks reproduction in animals under metabolic stress. Within the hypothalamus, energy deficits suppress gonadotropin-releasing hormone (GnRH) release from a sub-population of neurons that maintain fertility. Anorexia, cachexia, and excessive exercise suppress reproductive cyclicity in humans and with it the estrogen release essential for bone health. Fully 5% of women of reproductive age suffer from infertility related to eating disorders. Furthermore, the incidence of exercise-related anovulation may reach as high as 61% in gymnasts and 78% in runners. On the opposite end of the spectrum, obesity and diabetes also negatively affect fertility. As rates of these diseases rise, it is urgent that

we unravel the hypothalamic homeostatic mechanisms controlling body weight and fertility and the interactions between these two systems.

The hypothesis underlying my research is that circulating metabolic factors (such as leptin, insulin, ghrelin, glucose, LC-FAs or PYY_{3-36}) are perceived directly or indirectly by GnRH neurons of the hypothalamus and convey information that prevents GnRH release during a state of negative energy balance. Determining the mechanisms behind this metabolic-reproductive connection will provide much needed targets for medical treatment. The cornerstone of my laboratory's efforts is timed, targeted genetic manipulation using the power of tissue-specific gene deletion. Combined with anatomical, electrophysiological, and physiological techniques this approach offers a powerful tool for investigating the hypothalamic control of metabolism and fertility.

Terry D. Hinds, Jr., Ph.D., Assistant Professor - The focus of Dr. Hinds' research is on heme oxygenase (HO) reduction of obesity induced fatty liver, which can prevent cardiovascular disease. Diet induced obesity results in elevated levels of glucose and fatty acids in liver, resulting in enhanced production of reactive oxygen species (ROS). The heme oxygenase enzyme is functionally important for reducing ROS by increasing production of the antioxidant, bilirubin. His studies show that increasing HO activity attenuates the development of NAFLD in obese mice by significantly increasing expression of the nuclear receptor, peroxisome proliferator-activated receptor alpha (PPARalpha), resulting in the reversal of hepatic steatosis, increased energy expenditure, and decreased body weight. Dr. Hinds and co-workers have recently published a manuscript in the journal *Obesity,* elucidating the HO-1-PPARalpha-FGF21 axis as a new signaling paradigm that can manage obesity induced NAFLD, resulting in the lowering of cardiovascular disease.

Sudhir Jain, Ph.D., Assistant Professor - Human essential hypertension affects one billion people worldwide and is implicated in about 7 million deaths each year from ischemic heart disease and stroke. In United States, the prevalence of hypertension is 50% greater in blacks than in whites. In blacks, hypertension appears earlier, is generally more severe, and results in high rates of morbidity and mortality from stroke, heart failure, left ventricular hypertrophy, and end stage renal disease. Hypertension is a polygenic disease, and it has been estimated by segregation analysis and twin studies that approx. 45% of inter-individual differences in blood pressure can be accounted by genetic differences. In the past two decades, many genes that were implicated in simple (Mendelian) diseases have been identified by using genetic linkage and positional cloning methods. Although these methods have been remarkably successful in identifying high relative risk genes, they have not been successful in identifying genes that are involved in the complex forms of disease, such as hypertension and diabetes type-2. Moreover, hypertension is an arbitrary definition and not a quantitative trait that appears relatively late in life. Not much is known about the number of genes involved, their mode of transmission, their quantitative effect on blood pressure, their interaction with other genes, or their modulation by environmental factors. Parameters such as ethnicity and body weight increase the genetic heterogeneity and the difficulty of replication from one study to another. A number of whole-genome analyses have been

performed to identify different chromosomes involved in human hypertension. However, these studies are often non reproducible and genes involved in hypertension remain to be identified. Despite the characterization of cellular and physiological mechanisms that regulate blood pressure and alterations that contribute to hypertension, the genetic and molecular basis of this pathophysiology remains poorly understood.

Dr. Jain's current research interest is to understand molecular mechanisms involved in hypertension and hypertrophy with special emphasis on the role of the renin-angiotensin system (RAS) which plays an important role in the regulation of blood pressure. The Octapeptide Angiotensin-II is one of the most potent vaso-active substances known and is synthesized from its precursor molecule, angiotensinogen, which is primarily synthesized in the liver and to a lesser extent, in the kidney, brain, heart, adrenal, fat and vascular walls by the combined proteolytic action of renin and angiotensin converting enzyme. Recent studies have shown that patients with essential hypertension have higher plasma angiotensinogen levels and linkage studies have confirmed a direct relationship between angiotensinogen gene (AGT), its receptor gene AT1R and essential hypertension. However, molecular mechanisms involved in this process are not known. In addition, molecular mechanisms involved in tissue and hormone specific expression of these genes remain to be identified.

Bina Joe, Ph.D., FAHA, Professor – Dr. Joe's current research is focused on understanding the genetic component of blood pressure regulation using hypertensive rat models. Rat models serve as valuable alternatives to human studies for the identification and characterization of genetic factors/genes. The main strategy is to identify the disease causative genetic factor/gene based on its location on the rat genome by linkage analysis and substitution mapping. To this end, we have identified at least 16 different genomic regions that harbor quantitative trait loci (QTLs) for hypertension in rats. Recent integrated studies combining genetic and genomic approaches have resulted in the positional cloning of several novel genes implicated in BP control. Some of these are also detected to be linked to human essential hypertension. The expectation is to be able to translate our observations in rat models to disease causative mechanisms in humans.

Meenakshi Kaw, M.D., Ph.D., Assistant Professor – Dr. Kaw's research is focused on genetics of hypertension. Hypertension is one of the important components of metabolic syndrome. Obesity and metabolic syndrome is occurring in epidemic proportions now in adult population and is afflicting the children and young adults too. My interest in particular involves around the role of introns and promoter regions of angiotensinogen gene. We want to understand the role of single nucleotide polymorphisms in the angiotensinogen gene in the pathology of essential hypertension. In addition to genetics, I also want to understand the role of environment (diet, life style, and stress) in the occurrence of essential hypertension.

Sivarajan Kumarasamy, Ph.D., Assistant Professor - Essential hypertension is a classic example of a complex trait driven by environmental and genetic factors. However, the molecular basis of increased risk for developing hypertension remains

largely unknown. An animal model with a highly permissive hypertensive background would greatly aid in understanding the genetic causes for hypertension. The Dahl salt-sensitive rat is one such animal model, the genome of which has been compared and contrasted with that of several other rat strains to map multiple genomic segments as those harboring blood pressure (BP) quantitative trait loci. Among these mapped locations is a genomic segment on chromosome 9 that contains a highly prioritized positional candidate gene, Regulated Endocrine Specific Protein-18 (*Resp18*). *Resp18* is an intracellular signaling molecule that plays a role in the secretory pathway of peptidergic hormones. Further, the available literature indicates that *Resp18* could be functionally involved in BP regulation through its action on dopamine, which is a major regulator of salt and water reabsorption in the mammalian kidney. From recent literature evidence indicates that *Resp18* could be functionally involved in regulation of glucose metabolism. Despite this knowledge, the mechanism by which *Resp18* is involved in regulating blood glucose and BP remains unexplored. In order to understand the role of *Resp18* in BP regulation and glucose metabolism, novel $Resp18^{mutant}$ rat was created by using Zinc-Finger Nuclease method. Dr. Kumarasamy currently working on understanding the mechanistic aspects of *Resp18* gene in BP regulation and glucose metabolism using novel $Resp18^{mutant}$ rat model as a tool.

Ashok Kumar, Ph.D., F.A.H.A., Professor – Dr. Kumar's current research interest is to understand molecular mechanisms involved in hypertension and other cardiovascular diseases with special emphasis on the role of renin-angiotensin system. Angiotensin-II is one of the most potent vaso-active substances known and is synthesized from its precursor molecule, angiotensinogen, by the combined proteolytic action of renin and angiotensin converting enzyme. Recent studies have shown that patients with essential hypertension have higher plasma angiotensinogen levels and linkage studies have suggested an association between angiotensinogen gene and essential hypertension. However, molecular mechanisms involved in increased plasma angiotensinogen level in hypertensive patients have not been clarified. The human angiotensinogen gene contains six polymorphic sites located between one Kb of its promoter. Recent studies from our group have shown that these single nucleotide polymorphisms form distinct haplotypes that are associated with hypertension in Caucasian and African-American hypertensive subjects. Our recent studies have shown that certain haplotypes of human angiotensin receptor gene are also associated with essential hypertension especially in female Caucasian subjects. Our transient transfection and gel shift analyses have identified transcription factors that bind to these polymorphic sites so as to understand their role in transcriptional regulation.

In order to understand molecular mechanisms involved in hypertension in an *in vivo* situation, we have generated transgenic mice that contain wild type and modified BACs containing different haplotypes of human angiotensinogen and angiotensin receptor genes. These BACs (containing 160-180 Kb of DNA) presumably contain 50-80 Kb of the promoter sequences that are required for tissue specific expression of these genes but differ only in specific single nucleotide polymorphic sites. Therefore these transgenic mice are unique to understand the role of single nucleotide polymorphisms in the promoter region of these genes on transcriptional regulation in an *in vivo* situation.

Our studies have shown that certain haplotypes of angiotensinogen and angiotensin receptor genes increase the blood pressure in transgenic mice. Our *in vivo* chromatin immunoprecipitation studies have shown that increased blood pressure is correlated with increased transcription of these genes in the liver and kidney of transgenic mice. Since renin-angiotensin system plays an important role in hypertension as well as Cardiac Hypertrophy and Renal Disease, these transgenic mice will be useful to identify novel agents to reduce hypertension and other cardiovascular diseases.

Beata Lecka-Czernik, Ph.D., Professor - Diabetes, obesity, and osteoporosis are major public health concerns due to their prevalence in our increasingly sedentary and aging society. The peroxisome proliferator-activated receptor-gamma (PPARγ) transcription factor is a key regulator of glucose metabolism and energy expenditure. This protein also regulates lineage commitment of bone marrow mesenchymal stem cells (MSC). We have demonstrated that PPARg protein is involved in changing of MSC phenotype observed during aging and diabetic disease. Changes in the MSC phenotype include shifting of the MSC differentiation potential toward adipocyte (fat cells) and away of osteoblasts (bone forming cells), which leads to the bone loss with simultaneous accumulation of fat in bone cavities. PPARgamma protein is a target for a class of anti-diabetic drugs TZDs, which decrease glucose levels and increase insulin sensitivity. Although their beneficial anti-diabetic profile, prolonged treatment with these drugs leads to the bone loss and increased number of bone fractures in diabetic patients. We have demonstrated that similar to aging, TZDs affect bone mass by changing differentiation pattern of bone marrow MSC. The research in our laboratory is dedicated to: i) understanding and manipulating molecular mechanisms which are responsible for age- and diabetes-related changes in MSC potential to for new bone; ii) development of new methods to improve bone fracture healing in diabetic patients by means of stem cell-based and siRNA-based therapies; iii) testing of different methods of therapeutic interventions to prevent bone loss associated with an anti-diabetic TZD therapy.

Nikolai Modyanov, Ph.D., Professor – The overall goal of my current research is to understand the physiological role of the unique BetaM proteins encoded by ATP1B4 genes, which were originally discovered in my laboratory. We determined that ATP1B4 genes represent a rare instance of vertebrate gene co-option that radically changed functions of BetaM during the evolution. In lower vertebrates BetaM is a subunit of Na,K-ATPase. In placental mammals BetaM-proteins lost their ancestral functions and became the only currently known skeletal and atrial cardiac muscle-specific protein of the inner nuclear membrane, where it capable to function as a regulator of gene expression and signal transduction.

We developed *Atp1b4* knockout mouse model and determined that loss of BetaM resulted in growth retardation leading to high mortality of neonatal knockout mice. These findings point to the important role of BetaM in development of heart and skeletal muscles.

During the report period we have performed comparative analysis of gene expression in skeletal muscles of knockout and wild type neonatal male mice using mRNA-seq technology, which exposed a global picture of the effect of BetaM ablation on gene expression.

These experiments *revealed* strong down-regulation of fast-twitch and up-regulation of slow-twitch muscle genes. Most importantly, these experiments *also revealed* broad changes in expression of genes regulating lipid and fatty acid metabolism, thus indicating that BetaM is implicated in functions of skeletal muscle as endocrine organ.

Notably, Atp1b4 knockout males, which survived to adulthood, upon feeding by a high-fat diet showed far less weight gain, are resistant to diet-induced obesity, exhibit enhanced insulin sensitivity and improved glucose tolerance compared with wild type littermates. These robust changes in mouse metabolic parameters indicate a strong function of BetaM in energy expenditure pathways in muscle. Knowledge of BetaM functions may have significant implications for a better understanding of mechanisms underlying metabolic diseases such as diet-induced obesity and type 2 diabetes in humans.

These studies generated critically important preliminary data needed for successful submission of application to the recent NIH FOA, "*Functions of Skeletal Muscle beyond Contraction"*, which specifies support for exploratory projects focused on functions of skeletal muscle including its role in regulation of systemic metabolism as it relates to obesity and diabetes.

Brahma Raju Mopidevi, Ph.D., Assistant Professor - Hypertension is a serious risk factor for myocardial infarction, heart failure, vascular disease, stroke, and renal failure. Like other complex diseases, hypertension is caused by a combination of genetic and environmental factors. It has been estimated by segregation analysis and twin studies that approximately 45% of the inter-individual differences in blood pressure can be accounted by genetic differences. However, molecular mechanisms involved in pathophysiology of hypertension are not clear.

Aldosterone synthase, the rate limiting enzyme in the biosynthesis of aldosterone, is encoded by Cyp11B2 gene. This gene is expressed mainly in adrenal cortex and to some extent in kidney, brain, and adipose tissue. The epidemiological studies have suggested that -344T/C polymorphism is shown to be associated with increased aldosterone level and increased blood pressure. The hCyp11B2 gene has 3 SNPs in 1 Kb of its promoter and these polymorphisms are in almost complete linkage dis-equilibrium. These SNPs are rs1799998 (T/C at -344), rs10087214 (C/T at -470), and rs28659182 (C/A at -663). Thus variant -344T almost always occurs with variants -470C and -663A (named haplotype-I), and variant -344C almost always occurs with variants, -470T and -663T (named haplotype-II) in human subjects. In order to understand the physiological role of these haplotypes on transcriptional regulation of hCyp11B2 gene and blood pressure regulation in an *in vivo* situation, we have generated transgenic mice by *knocking in* hCyp11B2 gene containing either haplotype-I or haplotype-II at the HPRT locus. Currently our group actively engaged in studying the

molecular mechanism by which these promoter polymorphisms alter the binding of the transcription factors and regulate the blood pressure. Further we have extended our research interests to micro RNA and shown that the microRNA miR-31 and miR-584 bind strongly to the human angiotensinogen (hAGT) 3'UTR containing 11525C-allele as compared to 11525A-allele and down-regulate the hAGT mRNA and protein levels in human liver cells. These studies not only provide new insight into understanding the molecular basis of hypertension, but will also have significant clinical relevance to develop new therapeutic strategies for hypertension.

Sonia M. Najjar, Ph.D., Frederick W. Hiss Endowed Professor in Diabetes Research; Professor, Department of Physiology & Pharmacology and Director, CeDER - Dr. Najjar's research focuses on identifying the genetic and environmental interactions underlying obesity, type 2 diabetes and their cardiovascular complications, including atherosclerosis and hypertension.

The laboratory pioneered the finding that CEACAM1 plays a key role in regulating insulin action by promoting insulin clearance in liver. By generating mouse models of loss- or gain-of function of this protein, the Najjar team observed that genetic inactivation/deletion of this protein causes insulin resistance, obesity and fatty liver disease, in addition to predisposing to type 2 diabetes, Non-alcoholic steatohepatitis (NASH) and atherosclerosis. Using this model, the laboratory found that hyperinsulinemia causes insulin resistance and is not a marker thereof.

The Najjar laboratory also investigates the central role of CEACAM2 proteins in regulating energy balance and insulin secretion via regulating GLP1 secretion. Moreover, current studies focus on the role of CEACAM1 in linking the increase in common types of cancer in relationship with obesity.

Nitin Puri, M.D., Ph.D., Assistant Professor – Dr. Puri's research interest lies in the investigation of role of redox molecules in the (dys)functional regulation of cardio-vascular and metabolic homeostasis. We also examine the contributions of chronic oxidative stress and metabolic imbalance, as it pertains to the development of obesity and diabetes with associated long-term complications. In this regard, the principal focus of my investigation is the heme-heme oxygenase system. This antioxidant enzyme system is one of the principal cellular defenses against redox imbalance and also plays a central role in cardio-vascular function via its product generation, i.e. carbon monoxide and biliverdin. We have found that chronic oxidative stress has reciprocal effects on HO expression and activity; where a strong transcriptional activation of HO is seen by reactive oxygen species (ROS), emerging evidence shows an inhibitor effect of ROS on HO activity. In this context, we examine the differential cardio-vascular and metabolic effects of oxidants, including hydrogen peroxide and superoxide anion, in affecting HO system and examining how this translates to development of a clinical syndrome. Our experimental model systems include resistance arteries, animal models of hypertension (2K1C), animal models of diabetes and metabolic syndrome and *in vitro* models of human mesenchymal stem cells and mouse pre-adipocytes. Recently, we have shown that cellular overexpression of Sirt1 protects against patho-physiological effects of

oxidative stress and are currently exploring the regulatory crosstalk between HO system and Sirt1 & 6. An equally exciting focus my research entails examining HO-dependent regulation of eicosanoids and their physiological effects, particularly in the vasculature and perivascular adipocytes. We have made significant headway in this direction where we have shown existence of a feedback loop between epoxides and HO whose stimulation by either of the two systems attenuates oxidative stress and adipocyte dysfunction in *in vitro* as well as *in vivo* models.

Edwin R. Sanchez, Ph.D., Professor - Research in Dr. Sanchez's lab focuses on the nuclear receptors, with an emphasis on the tetratricopeptide repeat (TPR) proteins that act as molecular chaperones to the receptors. These chaperone proteins include: FK506-binding protein 52 (FKBP52), FKBP51, protein phosphatase 5 (PP5) and cyclophilin 40 (Cyp40).

Nuclear receptors act as hormone-activated transcription factors. Many important endocrine and physiological processes are controlled by these receptors, including immunity and inflammation, glucose and fatty acid metabolism, male and female reproduction, and blood pressure
Nuclear receptors can be activated by steroid hormones, such as progestins, estrogens, androgens, mineralocorticoids and glucocorticoids. But they can also be activated by a variety of lipophilic, organic molecules, such as fatty acids, prostaglandins and their derivatives. The central thrust of the research program is to understand how the TPR chaperones described above contribute to the actions of steroid receptors at the molecular, cellular and physiological level.

The most recent findings at the Sanchez laboratory suggest that the TPR chaperones act as tissue-selective modulators of steroid receptor physiology. FKBP52 was found to exert a stimulatory effect on progesterone receptor action only in the uterus and not in other female reproductive organs. Similarly, FKBP52 is needed for the androgen receptor contribution to embryonic development of select male reproductive organs, such as the prostate gland, but not others. Both FKBP51 and Cyp40 were found to be critically important to androgen receptor action in the adult prostate gland, and may be key factors necessary for the onset and progression of prostate cancer. Most recently, the laboratory has uncovered an interesting and unique reciprocal relationship between FKBP52 and FKBP51 on the activities of glucocorticoid receptor in liver, muscle and adipose tissues. Reciprocal modulation of the glucocorticoid receptor is such that these two chaperones serve to either increase or decrease the involvement of glucocorticoid receptors in development of metabolic syndrome and propensity to type 2 diabetes. In the case of FKBP51, we now know that it is also an essential regulator of the peroxisome proliferator-activated receptor (PPARγ), a nuclear receptor critically important to lipid metabolism and to the prevention of type 2 diabetes. FKBP51 promotes PPARγ activity by inhibiting the kinases which target PPARγ. More importantly, studies in cells and mice have shown that FKBP51 is essential for PPARγ mediated development of adipose tissue and the storage of lipid. Indeed, loss of FKBP51 protein in mice leads to greater insulin and glucose sensitivity, hallmarks of the "anti-diabetic" state. Interestingly, our studies with PP5 deficient cells and mice have

shown that this chaperone also regulates PPARγ. Not surprisingly, PP5 cells are resistant to differentiation into adipocytes and PP5 deficient mice are lean, with greatly reduced fat mass, are more insulin sensitive and exhibit highly elevated bone mineral density. These are all hallmarks of animals with a healthy lipid profile. Lastly, the laboratory has discovered a novel isoform of the glucocorticoid receptor (GRβ) in the mouse and its potential role in insulin action.

Taken as a whole, this investigative effort has identified TPR proteins as novel and potentially important targets for drug development against male and female infertility, prostate cancer, and metabolic disorders, such as diabetes and obesity.

John W. Turner, Jr., Ph.D., Professor – Dr. Turner's research focuses in 2 areas:
1) Development of biomarkers for environmental stress
2) Development of multi-year controlled-release contraceptive vaccines
Regarding biomarker studies, the effort is directed at the use of the stress hormone cortisol as a reference base for assessing effects of environmental stressors on gene expression, with emphasis on stress-related and reproduction-related genes. The experimental model is stress in fish associated with environmental compromises in coral reef ecosystems. These studies advance knowledge regarding stress and gene expression while addressing a critical problem of environmental stressors causing worldwide declines in coral reef ecosystems.

Regarding contraception studies, the effort is directed at multi-year contraception achieved with a single immunization and employs a polymer-based, controlled-release component in the vaccine to provide boostering. The controlled-release aspect allows for multiple boostering across a 3-20 month period and yields vaccines enduring for up to 3 years. The experimental model for these studies is the horse, with application to limit free-roaming wildlife populations to match their habitat capacity. Controlled-release boostering has potential for use with a number of animal and human vaccines. Expansion and updating of the *reefmonitor.org* website, which was launched by J. Turner and S. Sloan in February 2009 through iTunes U Ohio and was well used in 2013, is underway and will be completed by late 2014. It includes a 7-segment series on Coral Reef Ecology and a 6-segment series on Wild Horse Fertility Control. The iTunes U site offers >200,000 programs and our series has been as high as #11 in viewed programs in this list.

Continued development of a UT on-line course in coral reef ecology in collaboration with T. Bridgeman, PhD in the UT Dept. of Environmental Science and D. Bowers, MS Ed., Bellevue HS, OH. Administrative and curriculum issues dealt with in 2013 have led us to a revised expected staring date of Spring 2015.

Guillermo Vazquez, Ph.D., Associate Professor - Research in Dr. Vazquez's lab is focused on molecular and cellular aspects associated to the pathogenesis of atherosclerosis, with emphasis on the role of non-selective cation channels, such as Transient Receptor Potential Canonical (TRPC) channels and alpha-7 nicotinic acetylcholine receptors. Atherosclerosis is a disease of the arterial wall with a dominant

and maladaptive inflammatory response. It represents the major cause of coronary artery disease, the leading cause of death in western societies. In addition, atherosclerosis is the main vascular complication of metabolic diseases such as diabetes, obesity and metabolic syndrome. Over recent years Dr. Vazquez's group has discovered that endothelial TRPC3 channels are obligatory components of the signaling underlying regulated expression of cell adhesion molecules and monocyte recruitment to the subintima, two critical events throughout all stages of atherosclerotic lesion development. Dr. Vazquez's laboratory has also discovered a novel nicotinic acetylcholine receptor-dependent survival pathway in coronary endothelium. More recently, his lab has shown that TRPC3 contributes to mechanisms of macrophage survival and efferocytosis. Recent in vivo studies using a mouse model of atherosclerosis and a bone marrow transplantation strategy show that macrophage deficiency of TRPC3 improves indicators of plaque stability in advanced lesions, suggesting that TRPC3 could represent a promising molecular target in strategies aimed at stabilizing advanced lesions and minimizing the risk of acute coronary syndromes. To study this, our lab makes use of in vitro (primary and immortalized cell lines) and in vivo (global and conditional transgenic and knockout mice; bone marrow transplantation) models of endothelial and macrophage dysfunction, and a number of techniques (including patch-clamp electrophysiology, real-time camera-based fluorescence imaging, real-time amperometry, protein chemistry/molecular biology, morphometric and immunohistochemical analysis of atherosclerotic lesions in mice).

Zi-Jian Xie, Ph.D., Professor - The Na/K-ATPase in Signal Transduction and its significance in physiology, disease and drug development.

Research Results: These can be surmised from the list of publications shown in Section 6, "Publications". In that listing, please note the 34 papers published or in press during the year. Our faculty and students presented work at various national and international meetings, as represented by 25 published abstracts. We also published one book chapter and 3 expert reviews.

Research Goals and Future Plans: Each active researcher has his or her goals. These are not easily summarized. The departmental goals are to provide the support needed for the faculty and students to continue their work. In the coming year, with the naming of a permanent chair, we should look toward adding new faculty to sustain the research productivity which is so vital to the research and education missions of the university.

4c. Clinical Service – The department provides no clinical service

4d. ADMINISTRATIVE AND UNIVERSITY SERVICES, *and*

4d1. EXTRAMURAL SERVICE

Our service activities are enumerated below. Our department faculty provided service to the College of Medicine and Life Sciences, the Graduate School of Biomedical Sciences, and the University of Toledo. We also provided significant service to the scientific community.

University and Departmental Service Activities

Andrew Beavis, Ph.D., Professor

Block Director, Organ Systems
Track Director: Biomedical Sciences Graduate Program Cardiovascular and Metabolic Diseases Track
Chairman: Institutional Animal Care and Use Committee (IACUC)
Member: Medical School Admissions Committee
Member: Executive Curriculum Committee (COMLS)
Member: Graduate Executive Committee (COGS)
Member: Preclinical Curriculum Committee
Member: Graduate Student Advisory Committees (for 8 Students)
Course/Block Associate Director: Organ Systems
Course Director: Fundamentals of Pharmacology I
Course Director: Fundamentals of Pharmacology II
Course Director: Fundamentals of Pharmacology III

George T. Cicila, Ph.D., Associate Professor

Course Director: Basic Genetics (PHYA6010) (36 hr)
Member of IACUC Committee (42 hr)
Course Director: MSBS-MS Physiology (INDI5250) (40 hr)
Course Director: Human Physiology (PHSL5050) (34 hr)
Physician Assistant Program Advisory Committee (3 hr)

Jennifer Hill, Ph.D., Assistant Professor

College of Medicine Council Secretary/Treasurer (52 hr)
College of Medicine Council, Department of Physiology & Pharmacology Representative (5 hr)
CeDER Journal Club, Director (4 hr)
Interviewer, UT Medical School (3 hr)
Graduate Student Advisor: Latrice Faulkner and Mengjie Wang (200 hr)
CeDER Faculty Workshop, Director (1 hr)

Chair, Center for Diabetes and Endocrine Research (CeDER) steering committee (1 hr)
Thesis Advisory Committee Member: Latrice Faulkner, Simona Ghanem, Harshal Waghulde and Mengjie Wang (16 hr)

Terry Hinds, Ph.D., Assistant Professor

Mentoring

Medical Students:
James Raccuia
Luke O'Brien
Justin Baum
Jonathan Demeter
Maria Grabnar

Physician Assistant Students:
Bridger Butters

Ph.D. Student:
Lucien McBeth

Masters Students:
Yvette Unoarumhi
Kezia John

Bina Joe, Ph.D., Professor

Director, Center for Hypertension and Personalized Medicine
Graduate Students Admissions Committee
Faculty Rules and Regulations Committee, University of Toledo College of Medicine
LCME self study group member- FA-2, 5, 11 and 15
Major Advisor: Xi Cheng, Manish Sunder Karamchandani, Ying Nie, Resmi Pillai, Harshal Waghulde and Youjie Zhang
Thesis Advisory Committee Member for: Gaurav Mehta, Varunkumar Pandy, Prince Ampem, Sumit A. Solanki , Yanling Yan, Jiyoun Yeo and Xiaolu Zhang

Meenakshi Kaw, M.D., Ph.D., Assistant Professor

Mentoring M.S.B.S. students, M.D. students and Surf students, mentoring new postdoctoral students and lab assistants. Teaching them basic and translational research and how innovations in research can be applied to bed side in terms of new drug clinical trials.

Ashok Kumar, Ph.D., Professor

Department of Physiology and Pharmacology APT Committee (48 hr)
Director, CVMD Seminar Series

Beata Lecka-Czernik, Ph.D., Professor

Research Director and a Head of Steering Committee, Center for Diabetes and Endocrine Research (CeDER)
Promotion and Tenure Committee
Course Director Graduate Study, BMSP 632/832 System Pathophysiology II
Course Director, BRIM 620/820 Biomarkers Discovery, Validation and Implementation
Advisor for Ph.D. Candidates
Venkata Mantipragata (mentor Dr. Champa Jayasuriya, Dept. Orthopaedic Surgery)
Dulat Belboksynov, Cancer Biology Track (mentor Dr. Morrish, Dept. Cancer Biology)
Nabiyouni Maryam (mentor Dr. Sarit Baduri, Dept. Biomedical Engineering)

Nikolai Modyanov, Ph.D., Professor

Director of Graduate School Core Curriculum Course, "Current Problems and Research Approaches in Protein Structure and Catalysis" (120 hr)
Member of Institutional Animal Care and Use Committee (144 hr)
Co-chair of the Steering Committee (Center for Diabetes & Endocrine Research) (54 hr)
Member of 4 Graduate Student Advisory Committees (24 hr)

Sonia Najjar, Ph.D., Professor

<u>Administrative responsibilities</u>:

Director of the Center for Diabetes and Endocrine Research (CeDER)
For detailed activities as director of CeDER, please refer to the attached progress report

<u>Academic services</u>:

Ph.D. students mentorship:

Ph.D. mentor: Hilda Ghadieh, Simona Ghanem, Saja Khuder
Thesis Advisory Committee Member: Prabhatchandra R. Dube (a student of Dr. G. Vazquez), Nneka Mbah (a student of Dr. W. Maltese) and Mengjie Wang (a student of Dr. J. Hill)

Post-doctoral Fellowship mentoring:

Lucia Russo, Ph.D.: American Heart Association Post-doctoral fellowship

Summer Fellowship mentoring:

Jenny Brown (undergraduate student from California State University Monterey Bay (CSUMB) received an institutional summer undergraduate fellowship to carry out summer research project at the Najjar laboratory (Summer 2013).

Christopher Marino (UT medical student) received the institutional summer research fellowship to carry out his research project at the Najjar laboratory (Summer 2013).

Christopher Marino (UT medical student) received the 2014 summer research fellowship from the Endocrine Society to carry out his research project at the Najjar laboratory (Summer 2014).

Alexander Wisniewski (UT undergraduate student) received the First Year Summer Research Experience program (FYSRE) to carry out his research at the Najjar laboratory (Summer 2013).

Search Committees:

Search Committee for Chief of the Endocrine Division-Department of Medicine
Search Committee for Chief of Pediatric Endocrinology-Department of Pediatrics

Nitin Puri, M.D., Ph.D., Assistant Professor

Group & Individual discussions with medical, PA, MSBS and graduate students (60 hr)
Module Director Systems Pathophysiology I (12 hr)
Module Director Systems Pathophysiology II (12 hr)
Course Director Advanced Topics in CVMD (48 hr)
Contributions to the Peer Review Process (20 hr)

Howard Rosenberg, Ph.D., M.D., Professor and Interim Chairman

Interim Chair, Department of Physiology and Pharmacology
COMLS Student Promotions Committee
COMLS Admissions Committee
COMLS Pre-clinical Curriculum Committee
COMLS Executive Curriculum Committee
COMLS Executive Committee
Research Advisory Committee
Biomedical Sciences Graduate Executive Committee

Edwin Sanchez, Ph.D., Professor

Assistant Director, Center for Diabetes and Endocrine Research (CeDER) (400 hr)
Director, Cell Biology & Signaling Course
(attended by all Biomedical Sciences Graduate Students) (70 hr)
Director, Systems Pathophysiology II, CVMD Module (36 hr)
Dept. Phys. & Pharm. Appointment, Promotions & Tenure Committee (As needed)
Cardiovascular and Metabolism Diseases Program Steering Committee (As needed)
Ph.D. Advisory Committees (4) (40 hr)

John W. Turner, Jr., Ph.D., Professor

Department of Physiology and Pharmacology APT Committee (20 hr)
Department of Physiology and Pharmacology Curriculum Committee (30 hr)

Guillermo Vazquez, Ph.D., Associate Professor

Director, CVMD Seminar Series
Member, Council of the University of Toledo College of Medicine
Member, Advisory Committees: Qiming Duan, Sumit Monu, Resmi Pillai, Gurpanna Saggu and Harshal Waghulde
Member, BRIM Committee
Member, CVMD Admissions Committee
Membership Committee of the Graduate Council
Health Science Campus Graduate Executive Committee
Member, The University of Toledo Research Council

Zi-Jian Xie, Ph.D., Professor

COM Appointment, Promotions, and Tenure Committee
Member, Graduate Student Advisory Committees: Qiming Duan, Sumit Monu, Akshada Sawant, Moustafa Sayed and Jian Wu

4d1. EXTRAMURAL SERVICE

George T. Cicila, Ph.D., Associate Professor

Journal Peer Review: Hypertension

Kathirvel Gopalakrishnan, Ph.D., Assistant Professor

Judge at the 41st Annual Pharmacology Research Colloquium at Michigan State University, Lansing, MI, June 6, 2014.

Jennifer Hill, Ph.D., Assistant Professor

Ad hoc journal reviewing:

AJP: Regulatory, Integrative and Comparative Physiology
BBA Molecular Basis of Disease
Cell & Tissue Research
Cell Metabolism
Endocrine
Endocrinology
Experimental and Clinical Endocrinology & Diabetes
Frontiers in Neuroendocrinology
Journal of Endocrinology
International Journal of Fertility and Sterility
Neuroendocrinology
Neuropeptides
Obesity
Physiological Genomics
PLoS One
Reproductive Sciences

Editorial Board Member:

Frontiers in Systems and Translational Endocrinology, Guest Associate Editor, 2011-present

Terry Hinds, Jr., Ph.D., Assistant Professor

Editorial Board Member:

Diabetes Research
Obesity Research

Ad hoc Manuscript Review:

Hypertension

Sudhir Jain, Ph.D., Assistant Professor

Journal Reviewer:
American Journal of Hypertension
American Journal of Physiology: Heart and Circulatory Physiology
American Journal of Physiology: Endocrinology and Metabolism
American Journal of Physiology: Physiological Genomics
Molecular Biology Report
The Journal of Biological Chemistry

Bina Joe, Ph.D., Professor

Chief Editorial Positions:

Section Editor, Physiological Genomics - a Journal of the American Physiological Society; Section on "Molecular Genetics of Complex Traits"

Editorial Board Member:

Hypertension
International Scholarly Research Network (ISRN) Genomics
Global Science and Technology Forum Journal on Advanced Physiology Research

Journal Peer Review:

Nature
Genetics
Genomics
Hypertension
American Journal of Physiology-Renal Physiology
American Journal of Hypertension
American Journal of Physiology-Regulatory
Integrative and Comparative Physiology
Obesity Research
Critical Reviews in Biotechnology
Heredity
Diabetes
Critical Care Medicine
Clinica Chimica Acta
Mammalian Genome
Physiological Genomics
Journal of the American Society of Nephrology
Nephron
Journal of Biomedical Semantics
British Journal of Nutrition
PlosONE
Briefings in Bioinformatics
Clinical and Experimental Hypertension

Study Sections:

Ad hoc Member of the Genetics of Health and Disease study section of NIH
Program Project Review-Genes, Genomes and Genetics review group of NIH

International Thesis Evaluator:

Nitte University, Mangalore, India

Meetings Organized/Chair:

Chair, Trainee Highlight Session, Physiological Genomics group, APS, FASEB meeting, CA
Organizer, International Meeting-Rat Models and Genomics, Hinxton, United Kingdom.
Session Chair, Cardiovascular session, Rat Models and Genomics Meeting, Hinxton, United Kingdom
Session Chair, Genetics, Genomics, Proteomics and Metabolomics poster session, International Society of Hypertension-European Society of Hypertension Joint meeting, Athens, Greece

Sivarajan Kumarasamy, Ph.D., Assistant Professor

AHA Peer Reviewer:

Basic Cell, Cell Structure & Survival 1 Committee

Journal Reviewer:

Physiological Genomics, Hypertension, Diabetes Research and Clinical Practice

Other

Judge at the 41st Annual Pharmacology Research Colloquium at Michigan State University, Lansing, MI, June 6, 2014.

Ashok Kumar, Ph.D., Professor

Study Sections, Review Panels:

Ad Hoc Member: NIH: Heart, Blood and Lung Institute Study Section
Reviewer: Phillip Morris Research Grants
Reviewer: Wellcome Trust Grants
Ad. Hoc. Member: Study Section of American Heart Association
Member: Hypertension and Microcirculation study section of NIH
Ad. Hoc Member: GM study section of NIH

Journal Peer Review:

Journal of Biological Chemistry
American Journal of Hypertension
Hypertension
Hypertension Research
American Journal of Physiology
Nucleic Acids Research
Human Genetics

Beata Lecka-Czernik, Ph.D., Professor

Editor:

Journal of Postgenomics: Drug & Biomarker Development

Editorial Advisory Board:

Open Longevity Science

Editorial Board:

Adipocyte
PPAR Research

Book Editor:

Springer International Publishing
Diabetic Bone Disease – Basic and Translational Research and Clinical Applications

Bone
Guest Editor for Special Issue: Bone and Diabetes

Frontiers in Endocrinology

Editor for Bone Section

Reviewer for the following Peer Reviewed Journals

Nature Clinical Practice Endocrinology & Metabolism
Journal of Clinical Investigation
Journal of Bone and Mineral Research
Bone
Aging Research
Journal of Cellular Biochemistry

Molecular and Cellular Endocrinology
Calcified Tissue International

Study Sections, Review Panels

NIH/National Institute on Aging, Biological Aging Review Committee
(Isales Supplement)

NIH/National Institute on Aging, Special Emphasis Panel, ZAG1 ZIJ-8, Regulation of Bone Mass Accrual by Serotonin (Karsenty – PI)

NIH Fellowships Review Panel ZRG1 F06-P

NIH/National Institute on Aging, Clinical Aging Review Committee NIA-C

NIH/National Institute on Aging, Special Emphasis Panel, ZAG1 ZIJ-8 M3

Special/Invited Presentations at National and International Meetings

Session Chair and Speaker, 43rd International Sun Valley Workshop, Sun Valley, ID: *Inducible Brown Adipose Tissue or "beige" fat sensitizes to insulin and secretes bone anabolic activities* (August 2013)

16th International Congress of Endocrinology & 96th Annual Meeting of The Endocrine Society, Chicago, IL: *Marrow, Fat and the Skeleton* (June 2014)

Organizer and Speaker, ASBMR Topical Meeting "Bone and Diabetes", Houston, TX: *Fat Metabolic Status and Bone* (2014)

Invited Presentations

Wright State University, Dayton, OH: *PPARgamma nuclear receptor integrates bone with energy metabolism system* (November 2013)

Michigan State University, East Lansing, MI: *PPARgamma nuclear receptor integrates bone with energy metabolism system* (December 2013)

Nikolai Modyanov, Ph.D., Professor

Journal Peer Review:

Biochemistry
Molecular Pharmacology
Biochimica et Biophysica Acta (Bioenergetics, Biomembranes, Gene Structure and Expression)
FASEB Journal

Editorial Board:

Member of Editorial Board of "Biochemistry Research International"
Member of Editorial Board of "International Journal of Clinical Pharmacology and Toxicology (IJCPT)"
Member of Advisory Board of International Journal, "OA Biochemistry" (London, UK)
Associate Editor of International Journal “WSEAS Transactions on Biology and Biomedicine”
Member of Editorial Board of International Journal “Research Journal of Developmental Biology”
Associate Editor of “International Journal of Biology and Biomedical Engineering”

International Meetings Program or Advisory Committees:

3rd International Conference on Biomedicine and Health Engineering,
Tenerife, Spain (January 2014)

The 2014 International Conference on Biology and Biomedical Engineering.
Venice, Italy (March 2014)

The 2014 International Conference on Biology and Biomedicine,
Prague, Czech Republic (April 2014)

5th International Conference on Bioscience and Bioinformatics (ICBB '14),
Gdansk, Poland (May 2014)

2nd International Conference on Biology, Medical Physics, Medical Chemistry, Biochemistry and Biomedical Engineering, Beijing, China, 2014

Sonia Najjar, Ph.D., Professor

Academic Board Membership:

Member, Authority Board Edison Biotechnology Institute (EBI), Athens, OH
Member, External Advisory Committee, Diabetes Institute at Ohio Univ., Athens, OH

Academic Consulting:

American University of Beirut, Establishing the Middle East Diabetes Research Center

Board Membership in Professional Associations:

Board member, Juvenile Diabetes Research Foundation local chapter

Membership in Professional Associations:

Endocrine Society
American Diabetes Association
American Society for Biochemistry and Molecular Biology- Federation of American Societies for Experimental Biology
American Physiological Society
American Liver Foundation

Grant Reviewing Activities:

NIH Study Sections (Ad Hoc):

NIH- ZRG1 F06-T 20 L., Fellowships: Endocrinology, Metabolism, Nutrition and Reproductive Sciences
NIH-NIDDK: Molecular and Cellular Endocrinology Study Section Endocrinology, Metabolism, Nutrition and Reproductive Sciences IRG (EMNR)
NIDDK DDK-B1 Section; Diabetes, Endocrinology and Metabolic Diseases B Subcommittee
NIH-NIDDK: Fellowships: Endocrinology, Metabolism, Nutrition and Reproductive Sciences 2014/05 ZRG1 F06-T (20) L

NIH Study Sections (Standing member):

Program Advisory Council, NIH-supported Michigan Diabetes Research and Training Center (MDRTC) and the Michigan Center for Diabetes Translational Research's (MCDTR) Pilot and Feasibility Program (P/FS)
NIH-NIDDK: Hepatobiliary Pathophysiology Study Section

International Panels:

National Priorities Research Program (NPRP), Qatar National Research Fund, **Qatar**
Scientific Research Support Fund, **Jordan**

Editorial Board:

Honorary Editorial Board Member: "Hepatic Medicine: Evidence and Research"
International Scholarly Research Network-Hepatology
Topic editor: Molecular Metabolism

Manuscript Reviews:

American Journal of Physiology
Biochemistry
Cell Metabolism
Diabetes
Endocrinology
Gastroenterology
Hepatology
Journal of Biological Chemistry
Journal of Cellular Biochemistry
Journal of Cellular Physiology
Journal of Clinical Investigation
Journal of Endocrinology
Molecular Cancer
Molecular Endocrinology
Oncogene
PLOS ONE

Annual Meetings Abstract Reviewing Activities:

American Association Diabetes Annual Meeting

Invited Talks at International Meetings:

Speaker in 24th International CEA Workshop, Wakayama, **Japan**

Meet the Professor session, 24th International CEA Workshop, Wakayama, **Japan**

Chairperson at International Meetings:

The Endocrine Society Meetings: Insulin Secretion Symposium**,** Chicago, IL
Chair of "Diapers and Diabetes", Juvenile Diabetes Research Foundation, MI

Invited Institutional Seminars:

Brown University Department of Medicine

Nitin Puri, M.D., Ph.D., Assistant Professor

Peer Review Contributions:

Editorial Board Member: Journal of Hypertension and Cardiology

Peer review process:

Ad hoc manuscript reviewer for the American Journal of Physiology-heart and circulatory physiology
Ad hoc manuscript reviewer for the International Journal of Hypertension
Ad hoc manuscript reviewer for the Journal of Prostaglandins and Other Lipid Mediators
Ad hoc manuscript reviewer for the Journal of Biological Chemistry

Edwin Sanchez, Ph.D., Professor

Editorial Boards:

Journal of Steroid Biochemistry and Molecular Biology
Hormone Molecular Biology and Clinical Investigation
Nuclear Receptor Research
Steroids

Paper Reviews:

Biochemistry
Hormone Molecular Biology and Clinical Investigation
Journal of Cell Science
Steroids
Nuclear Receptor Research

Grant Reviews:

NIH Special Emphasis Panel – Career Awards (K Applications) (ad hoc)

Invited to speak at the University of Michigan:
"Nuclear Receptor Chaperones: Fulcrums of Molecular and Metabolic Equilibria".
Department of Pharmacology, University of Michigan, Ann Arbor, MI, December 2013.

John W. Turner, Jr., Ph.D., Professor

Wildlife Management Consultant

1. Virgin Islands National Park, United State Virgin Islands (coral reefs)
2. Barbuda and Antigua (feral donkeys)
3. Assateague Island National Seashore (wild horses)
4. US Forest Service: Jareta Mesa, NM; Montgomery Pass, CA (wild horses)
5. U.S. Department of Interior, Bureau of Land Management, National Wild Horse and Burro Program (wild horses)
6. Several Ohio municipalities (white-tailed deer)

Animal Care Committee member, Toledo Zoological Society
Toledo Zoo Programs Committee member
Marine Research Permitee, Commonwealth of the Bahamas

Research Reviewer:

Ad Hoc Peer Reviewer, National Science Foundation (NFS)
Ad Hoc Peer Reviewer, U.S. Department of Agriculture Small Grants Program
Peer Reviewer, NSF, Marine Sciences Program
Peer Reviewer, U.S. Department of Agriculture, SBIR Wildlife Program

Guillermo Vazquez, Ph.D., Associate Professor

Editorial Service:

Managing Editor, Frontiers in Bioscience
Editorial Board Member, Frontiers in Bioscience
Editorial Board Member, Cardiovascular and Hematological Agents in Medicinal Chemistry

Ad hoc reviewer for:

European Journal of Neuroscience
Cancer Therapy
Neuroscience
FEBS Letters
Journal of Biological Chemistry
Journal of Cellular and Molecular Medicine
Arteriosclerosis Thrombosis and Vascular Biology
Circulation Research

5. SUMMARY AND ASSESSMENT OF DEPARTMENT'S PRODUCTIVITY BASED ON THE FACULTY EFFORT REPORTS

As a group, we made considerable contributions in teaching, research and service to the institution and to the scientific community. Among the accomplishments are 34 published papers as well as book chapters, expert reviews and published abstracts, with many additional manuscripts in various stages of preparation or under review. Our research was supported by extramural funds, with $3,730,999 in research expenditures from extramural funding. The graduate program continued to enjoy success, and we had six newly-graduated doctoral students. We also provided successful teaching and leadership in several U.T. educational programs, and were actively involved in the university and scientific communities. Several members of the department have accomplishments in multiple areas, while others were more focused on one or a few aspects of our collective work. Everyone has made an honest effort at being a productive and valued part of our academic community. As a group, we can be proud of our accomplishments.

6. PUBLICATIONS AND GRANTS

Published Manuscripts

1. Abdul-Majeed, S., Mell, B., Nauli, S.M. and **Joe, B.** (2014) Cryptorchidism and infertility in rats with targeted disruption of the Adamts16 locus. *Plos One*, 9:e100967. PMID 24983376

2. Aboualaiwi, W.A., Muntean, B.S., Ratnam, S., **Joe, B.**, Liu, L., Booth, R.L., Rodriguez, I., Herbert , B.S., Bacallao, R.L., Fruttiger, M., Mak, T.W., Zhou, J., and Nauli, S.M. (2014) Survivin-induced abnormal ploidy contributes to cystic kidney and aneurysm formation. *Circulation* **129**:660-672, PMID: 24235270

3. Alshahrani, M.M., Yang, E., Yip, J., Ghanem, S.S., Abdallah, S.L., DeAngelis, A.M., O'Malley, C.J., Moheimani, F., **Najjar, S.M.**, and Jackson, D.E. (2014) CEACAM2 negatively regulates hemi (ITAM-bearing) GOVI and CLEC-2 pathways and thrombus growth *in vitro* and *in vivo*. *Blood, in press.*

4. Dowling, A.R., Nedorezov, L.B., Qiu, X., Marino, J.S., and **Hill, J.W.** (2013) Genetic factors modulate the impact of pubertal androgen excess on insulin sensitivity and fertility. *PLoS One*. **8**:e79849, PMID: 24278193

5. Drummond, C.A., Buddny, G., Haller, S.T., Liu, J., Yan, Y., **Xie, Z.**, Malhotra, D., Shapiro, J.I., and Tian, J. (2013) Gender differences in the development of uremic cardiomyopathy following partial nephrectomy: Role of progesterone. *J. Hypertens.* **31**:2. PMID: 24404431

6. Drummond, C.A., Sayed, M., Evans, K.L., Shi, H., Wang, X., Haller, S.T., Liu, J., Cooper, C.J., **Xie, Z.**, Shapiro, J.I. and Tian, J. (2014) Reduction of Na/K-ATPase

affects Cardiac Remodeling and Increases c-kit cell abundance in Partial Nephrectomized Mice. *Am. J. Physiol. Heart Circ. Physiol.* **306**:H1631-H1643.

7. Ebke, L.A., Nestor-Kalinoski, A.L., Slotterbeck, B.D., Al Dieri, A.G., Ghosh-Lester, S., Russo, L., **Najjar, S.M.,** von Grafenstein, H., and McInerney, M.F. (2013) Tight Association between Macrophages and Adipocytes in Obesity: Implications for Adipocyte Preparation. *Obesity* **22**:1246-55. PMID: 24376179

8. Gable, M.E., Abdallah, S.L., **Najjar, S.M.,** Liu, L., and Askari, A. (2014) Digitalis-induced cell signaling by the sodium pump: on the relation of Src to Na+/K+-ATPase (2014) *Biochem. Biophys. Res. Commun*. **446**:1151-1154. PMID: 24667596.

9. **Hinds, T.D., Jr.**, Stechschulte, L.A., Elkhairi, F., Gold, B.G., and **Sanchez, E.R.** (2014) Analysis of FK506, Timcodar (VX-853) and FKBP51 and FKBP52 Chaperones in Control of Glucocorticoid Receptor Activity and Phosphorylation. *Pharmacology Research & Perspectives*, *in press*.

10. **Jain, S.**, Prater, A., Pandey, V.G, Rana, A., **Puri, N.**, and **Kumar, A.** (2013) A Haplotype of Angiotensin Receptor Associated with Human Hypertension Increases Blood Pressure in Transgenic Mice. *J. Biol. Chem.* **288**:37048-37056. PMID: 24202179

11. Kathem, S.H., Mohieldin, A.M., Abdul-Majeed, S., Ismail, S.H., Altaei, Q.H., Alshimmari, I.K., Alsaidi, M.M., Khammas, H., Nauli, A.M., **Joe, B.**, and Nauli, S.M. (2014) Ciliotherapy: a novel intervention in polycystic kidney disease. *J. Geriatr. Cardiol.* **11**:63-73. PMID: 24748884

12. Khundmiri, S.J., Salyer, S.A., Farmer, B., Qipshidze-Kelm, N., Murray, R.D., Clark, B.J., **Xie, Z.**, Pressley, T.A., and Lederer, E.D. (2014) Structural determinants for the ouabain-stimulated increase in Na-K ATPase activity. *Biochim. Biophys. Acta.* **1843**:1089-102. PMID: 24566089

13. Kim, J.H., Meyers, M.S., Khuder, S.S., Abdallah, S.L., Muturi, H.T., Russo, L., Tate, C.R., Hevener, A.L., **Najjar, S.M.,** Leloup, C., and Mauvais-Jarvis, F. (2014) Tissue-selective estrogen complexes with bazedoxifene prevent metabolic dysfunction in female mice. *Mol. Metab.* **3**:177-90. PMID: 24634829.

14. Kolli, V., Stechschulte, L.A., Dowling, A.R., Rahman, S., Czernik, P.J., and **Lecka-Czernik, B.** (2014) Partial agonist, telmisartan, maintains PPARγ serine 112 phosphorylation, and does not affect osteoblast differentiation and bone mass. *PlosOne* **9**:e96323. PMID: 24810249.

15. Korneenko, T.V., Pestov, N.B., Okkelman, I.A., and **Modyanov, N.N.,** Shakhparonov, M.I. (2014) P4-ATP-ase Atp8b1/FIC1: structural properties and (patho)physiological functions. *Russian J. Bioorgan. Chem., in press*.

16. Lai, F., Madan, N., Ye, Q., Duan, Q., Li, Z., Wang, S., Si, S., and **Xie, Z.** (2013) Identification of a mutant α1 Na/K-ATPase that pumps but is defective in signal transduction. *J. Biol. Chem., in press*.

17. **Lecka-Czernik, B.** and Fowlkes, J. (2013) *Bone and Diabetes*. Meeting report from the 43rd International Sun Valley Workshop. *IBMS BoneKEY* **10**:429, doi:101038/bonekey.2013.163

18. Lee, R.H. and **Vazquez, G** (2013) Evidence for a prosurvival role of alpha-7 nicotinic acetylcholine receptor in alternatively (M2) activated macrophages. *Physiol. Rep.* 1:e00189. PMID: 24744866.

19. Makani, V., Sultana, R., Sie, K.S., Orjiako, D., Tatangelo, M., Dowling, A., Cai, J., Pierce, W., Butterfield, D.A., **Hill, J.**, and Park, J. (2013) Annexin A1 Complex Mediates Oxytocin Vesicle Transport. *J. Neuroendocrinol.* 12:1241-1254. PMID: 24118254

20. Marino, J.S., **Hinds, T.D., Jr.**, Potter, R.A., Ondrus, E., Onion, J.L., Dowling, A., McLoughlin, T.J., **Sanchez, E.R.**, and **Hill, J.W.** (2013) Suppression of protein kinase C theta contributes to enhanced myogenesis *in vitro* via IRS1 and ERK1/2 phosphorylation. *BMC Cell. Biol.* **14**:39. PMID: 24053798

21. Mehotra, A., **Joe, B.** and de la Serna, I.L. (2013) Enhanced SWI/SNF enzyme recruitment and chromatin remodeling on fetal cardiac gene promoters is associated with cardiac hypertrophy in a genetic rat model of hypertension. *J. Cell. Physiol., in press*. PMID: 23702776.

22. Mell, B., Abdul-Majeed, S., **Kumarasamy, S.**, Waghulde, H., Pillai, R., Nie, Y. and **Joe, B.** (2014) Multiple blood pressure loci with opposing blood pressure effects on rat chromosome 1 in a homologous region linked to hypertension on human chromosome 15. *Hypertension Research, in press.*

23. Pereira, S., Park, E., Mori, Y., Haber, C.A., Han, P., Uchida, T., Stavar, L., Oprescu, A.I., Koulajian, K., Ivovic, A., Yu, Z., Li, D., Bowman, T.A., Dewald, J., El-Benna, J., Brindley, D.N., Gutierrez-Juarez, R., Lam, T.K.T., **Najjar, S.M.,** McKay, R.A., Bhanot, S., Fantus, I.G., and Giacca, A. (2014) FFA-induced Hepatic Insulin Resistance *in vivo* is mediated by PKC-δ, NADPH Oxidase, and Oxidative Stress. *Am. J. Physiol. Endocrinol. Metab.* **307**:E34-46. PMID: 24824652

24. Pillai, R., Waghulde, H., Nie, Y., **Gopalakrishnan, K.**, **Kumarasamy, S.**, Farms, P., Garrett, M.R., Atanur, S.S., Maratou, K., Aitman, T.J. and **Joe, B.** (2013) Isolation and high-throughput sequencing of two-closely linked epistatic hypertension susceptibility loci with a panel of bicongenic strains. *Physiol Genomics.* **45**:729-736. PMID: 23757393.

25. Rapp, J.P., and **Joe, B**. (2013) Do epistatic modules exist in the genetic control of blood pressure in Dahl rats? A critical perspective. *Physiol Genomics* **45**:1193-1195, PMID: 24192392

26. Sodhi, K., **Puri, N.**, Kim, D.H., **Hinds, T.D., Jr.,** Stechschulte, L.A., Favero, G., Rodella, L., Shapiro, J., Jude, D., and Abraham, N. (2014) PPAR-delta Binding to Heme Oxygenase 1 Promoter Prevents Angiotensin II Induced Adipocyte Dysfunction in Goldblatt Hypertensive Rats. *Int. J. Obes. (Lond).* 38:456-65. PMID: 23779049

27. Solanki, S., Dube, P., Tano, J.Y., Birnbaumer, L., and **Vazquez, G.** (2014) Reduced endoplasmic reticulum stress-induced apoptosis and impaired unfolded protein response in TRPC3 deficient M1 macrophages. *American Journal of Physiology-Cell Physiology, in press*.

28. Stechschulte, L.A., **Hinds, T.D., Jr.**, Khuder, S.S., Shou, W., **Najjar, S.M.**, **Sanchez, E.R.** (2014) FKBP51 Controls Cellular Adipogenesis Through p38 Kinase-mediated Phosphorylation of GRα and PPARγ. *Mol. Endocrinol.* **28**:1265-1275. PMID: 24933247

29. Stechschulte, L.A., **Hinds, T.D., Jr.**, Khuder, S.S., Shou, W., **Najjar, S.M.**, and **Sanchez, E.R.** (2014) FKBP51-mediated Phosphorylation of GRα and PPARγ Regulates Cellular Adipogenesis. *Mol. Endocrinol., in press.*

30. Stechschulte, L.A., **Hinds, T.D., Jr.**, Ghanem, S.S., Shou, W., **Najjar, S.M.**, and **Sanchez, E.R.** (2014) FKBP51 Reciprocally Regulates GRα and PPARγ Activation via the Akt-p38 Pathway. *Mol. Endocrinol., in press.*

31. Stechschulte, L.A., Wuescher, L, Marino, J., **Hill, J.**, Eng, C., and **Hinds, T.D., Jr.** (2014) Glucocorticoid Receptor β Stimulates Akt1 Growth Pathway by Attenuation of PTEN. *J. Biol. Chem*. PMID: 24817119

32. Tano, J.Y., Solanki, S., Lee, R.H., Smedlund, K., Birnbaumer, L., and **Vazquez, G.** (2014) Bone marrow deficiency of TRPC3 channel reduces early lesion burden and necrotic core of advanced plaques in a mouse model of atherosclerosis. *Cardiovascular Research* **101:**138-144. PMID: 24101197

33. Wang, Y., Ye, Q., Liu, C., **Xie, J.X.**, Yan, Y., Lai, F., Duan, Q., Li, X., Tian, J., and **Xie, Z.** (2014) Involvement of Na/K-ATPase in hydrogen peroxide-induced activation of the Src/ERK pathway in LLC-PK1 cells. *Free Radic. Biol. Med.* **71**:415. PMID: 24703895

34. **Xie, J.X.**, Li, X., and Xie, Z. (2013) Regulation of renal function and structure by the signaling Na/K-ATPase. *IUBMB Life* **65**:991-8. PMID: 24323927

CHAPTERS IN BOOKS

Bourey, R.E., Kaw, M.K., Lesler, S.G., Ghanem, S.S., and **Najjar, S.M.** (2014) Diabetes. In: Diet, Exercise, and Chronic Disease: The Biological Basis of Prevention. pp: 76-96 (C. Murray Ardies, Ed). CRC Press; Taylor and Francis Group, Boca Raton.

REVIEWS

1. **Lecka-Czernik, B.** and Stechschulte, L.A. (2014) Bone and Fat: A Relationship of Different Shades. *Archives of Biochemistry and Biophysics.* [Epub ahead of print].

2. **Najjar, S.M.**, and Russo L. (2014) CEACAM1 loss links inflammation to insulin resistance in obesity and non-alcoholic steatohepatitis (NASH). *Semin Immunopathol.* Jan; **36(1)**:55-71. doi: 10.1007/s00281-013-0407-3. Epub. PMID: 24258517.

3. **Turner, J.W., Jr.** (2013) From the Pens to the Field: Real World Wildlife Contraception. *Journal of Zoo and Wildlife Medicine* 45S: S102-S110.

ABSTRACTS

1. de la Serna, I.L, Ahmad, N., Russo, L., Marathe, H.G., Pestov, N.B., **Najjar, S.M.**, and **Modyanov, N.N.** (2014) Evolutionarily acquired functions of eutherian BetaM, a muscle-specific protein of inner nuclear membrane. Poster Presentation. Keystone conference "Growth and Wasting in Heart and Skeletal Muscle", January, 2014, abstract #2021 page 54.

2. Doctor, D. (2013) The Role of Hypothalamic Leptin and Insulin Signaling in Reproduction, a Medical SURF Student in **Dr. Jennifer Hill's** Lab, at the Medical Student Research Forum, July 26, 2013.

3. Faulkner, L., Dowling, A., Stuart, R.C., Nillni, E.A., and **Hill, J.W.** (2014) Reduced melanocortin production underlies impaired mating behavior in males with neuronal insulin and leptin insensitivity. Poster, Michigan Diabetes Research Center Annual Symposium, University of Michigan, Ann Arbor, MI, April 2014.

4. Faulkner, L., Stuart, R.C., Nillni, E.A., and **Hill. J.W.** (2014) Disrupted Melanocortin Signaling Facilitates Type 2 Diabetes Associated Erectile Dysfunction. Poster, Keystone Conference on Obesity: A Multisystems Perspective, January 2014.

5. Faulkner, L.D., Stuart, R., Nillni, E.A. and **Hill, J.W.** (2014) Poster Disrupted Melanocortin Signaling Facilitates Type 2 Diabetes Associated Erectile Dysfunction, Endocrine Society Annual Meeting, June 2014.

6. **Gopalakrishnan**, **K.**, **Kumarasamy**, **S.**, Mell, B., and **Joe, B.** (2013) A novel long noncoding RNA targeting rififylin is mechanistically linked to the regulation of blood pressure, cardiac function and survival in a rat genetic model of hypertension. Cold Spring Harbor International "Rat Genomics and Models" meeting, New York, NY, December 11-14.

7. **Jain, S.**, Tulsulkar, J., Rana, A., Shah, Z.A., and **Kumar, A.** (2014) Transgenic mice containing haplotype-I of human angiotensin receptor type-1 gene are susceptible to stroke. HBPR, San Francisco, CA, September.

8. **Joe, B**. (2013) Fine-mapping a blood pressure quantitative trait locus on rat chromosome 1 by substitution mapping identifies two closely linked genomic segments with opposing bp effects. Cold Spring Harbor International "Rat Genomics and Models" Meeting, New York, USA, December 11-14.

9. **Kaw, M.K.**, Pandey, V., **Jain, S.**, **Puri, N.**, Rana, A., **Mopidevi, B.**, and **Kumar, A.** (2014) Dexamethasone Promotes Hypertension By Allele-Specific Regulation Of The Human Angiotensinogen Gene. HBPR, San Francisco, CA, September.

10. **Kumarasamy**, **S.**, **Gopalakrishnan, K.**, Abdul-majeed, S., and **Joe, B.** (2013) Zinc-finger nuclease mediated disruption of the regulated endocrine specific protein (resp18) locus lowers blood pressure of the hypertensive Dahl rat. Cold Spring Harbor International "Rat Genomics and Models" Meeting, New York, NY, December 11-14.

11. **Kumarasamy**, **S.**, **Gopalakrishnan, K.**, Mell, B., Morgan, E., Waghulde, H., and **Joe, B. (2013)** Targeted disruption of a GWAS prioritized candidate transcription factor, nr2f2, lowers blood pressure in a rat genetic model of hypertension. Cold Spring Harbor International "Rat Genomics and Models" Meeting, New York, NY, December 11-14.

12. Lamouroux, C., **Modyanov, N.**, and Crambert, G. (2014) Role of the H,K-ATPase type 2 in the regulation of blood pressure during K^+ depletion (860.8) Poster presentation. Experimental Biology, *FASEB J April 2014* 28:860.8.

13. Mell, B., **Kumarasamy, S.**, Abdul-majeed, S., Waghulde, H., Pillai, R., Nie, Y., and **Joe, B**. Fine-mapping a blood pressure quantitative trait locus on rat chromosome 1 by substitution mapping identifies two closely linked genomic segments with opposing bp effects. Cold spring harbor international "Rat Genomics and Models" meeting, New York, USA (11-14th December, 2013).

14. **Modyanov, N.N**., de la Serna, I.L, Ahmad, N., Russo, L., Archambeau, A.J, Pestov, N.B., **Najjar, S.M.**, and Michele, D.E. (2014) Evolutionarily acquired functions of BetaM as a muscle-specific regulator of metabolic gene expression, **New Directions in Biology and Disease of Skeletal Muscle Conference.** Abstract # 92, Chicago, June 2014.

15. **Modyanov, N.,** Korneenko, T., Shakhparonov, M., and Pestov, N. (2014) Conserved polarization of Na,K-ATPase in vertebrate skin epithelia (895.1) Poster presentation. Experimental Biology, *FASEB J*, *April 2014* 28:895.1.

16. **Mopidevi, B.**, **Kaw, M.**, Puri, N., Ponnala, M., and **Jain, S.**, Rana, A., Keetha, N.R., Fiering, S., and **Kumar, A.** (2014) A Genetic Variant of Human Aldosterone Synthase Gene Causes Salt-Dependent High Blood Pressure in Transgenic Mice. HBPR, San Francisco, CA, September.

17. Nie, Y., **Kumarasamy, S.**, Cheng, X., Mell, B., Pillai, R., Waghulde, H., Farms, P., and **Joe, B.** (2013) Mapping blood pressure QTLs on rat chromosome 9: Evidence for epistasis and putative epigenetic mechanisms. Cold Spring Harbor International "Rat Genomics and Models" Meeting, New York, NY, December 11-14.

18. Pestov, N.B., Korneenko, T.V., and **Modyanov N.N.** (2014) Matricide in Caenorhabditis elegans – a suicidal life span program alternative to aging. Poster Presentation. Keystone conference "Aging - Pushing the Limits of Cellular Quality Control", January, 2014, abstract #2021 page 54.

19. Pillai, R., **Kumarasamy, S.**, Nie, Y., Waghulde, H., **Joe, B.** (2013) Mapping a novel blood pressure quantitative trait locus within a congenic strain spanning a segment containing no known rat annotations. Cold Spring Harbor International "Rat Genomics and Models" Meeting, New York, NY, December 11-14.
20. Rana, A., **Jain, S.**, **Puri, N.**, **Kaw, M.K.**, and **Kumar, A.** (2014) Haplotype-dependent differential regulation of the human AT1R gene is exacerbated by age: effects on tissue inflammatory and redox milieu. HBPR, San Francisco, CA, September.

21. Stechschulte, L.A., **Hinds, T.D., Jr.**, Warrier, M., **Najjar, S.**, and **Sanchez, E.R.** (2013) FKBP51 chaperoning of GR and PPARg is required for diet-induced visceral adiposity and cellular adipogenesis. ENDO 2013, San Francisco, CA. Featured Poster. Oral Presentation, June.

22. Stechschulte, L.A., **Hinds, T.D., Jr.**, Warrier, M., **Najjar, S.**, and **Sanchez, E.R.** (2013) FKBP51 chaperoning of GR and PPARg is required for diet-induced visceral adiposity and cellular adipogenesis. ENDO 2013, San Francisco, CA. Featured Poster. Poster Presentation, June.

23. Stechschulte, L.A., **Hinds, T.D., Jr.**, **Najjar, S.M.**, **Lecka-Czernik, B.**, and **Sanchez, E.R.** (2014) Targeting Obesity and Osteoporosis through PP5 and FKBP51 Chaperoning of Nuclear Receptors. Nuclear Receptors: Biological Networks, Genome Dynamics and Disease (Keystone Symposia), Taos, NM, January.

24. Stechschulte, L.A., **Sanchez**, **E.R.**, Czernik, P.J., and **Lecka-Czernik, B.** (2014). The molecular chaperones Protein Phosphatase 5 (PP5) and FK506 Binding Protein 51 (FKBP51) regulate energy metabolism and bone mass by controlling PPARg activity in adipocytes and marrow mesenchymal stem cells. 41st Annual Pharmacology Colloquium. Michigan State University, Lansing, MI, Poster Presentation, June.

25. Thouennon, E., Cheng, Y., **Lecka-Czernik, B.,** and Loh, Y.P. (2013) Rosiglitazone, A PPARγ agonist, promotes neuronal survival by up-regulating neuroprotective protein carboxypeptidase E expression. 95th Annual Meeting, Endocrine Society.

GRANTS

New Grants and Competing Renewals Awards July 1, 2013 – June 30, 2014

PI: **Jennifer W. Hill**
Co-Investigator: Stanislaw Stepkowski
Agency: Michigan Diabetes Research Pilot/Feasibility Study Grant
Grant Number: N-124156-01
"Inflammatory processes driving insulin resistance in polycystic ovary syndrome."
Period of Support: 01/01/2014-12/31/2014
Total Costs: $36,000
Disposition: Funded

PI: **Bina Joe**
Agency: NIH/NHLBI
Grant Number: RO1- HL020176-36
Period of Support: 09/01/13 – 08/31/2018
Annual Award excluding indirect costs: $376,531
CSR-IRG review completed; Percentile scored = 4
Disposition: Funded

PI: **Ashok Kumar**
Agency: NIH
Grant Number: N-124065-01
Period of Support: 8/1/2014-5/31/2018
Annual Award Excluding indirect costs: $417,427
Disposition: Funded

Continuing Grant

PI: **Latrice Faulkner**, Graduate Student
Sponsor: **Jennifer W. Hill**
Agency: NIH
Grant Number: F31-HD-75608-02
Period of Support: 01/01/2013 – 02/28/15
Annual Award excluding indirect costs: $42,676
Disposition: Funded

PI: **Jennifer W. Hill**
Agency: NIH
Grant Number: R21-HD-071529-02
Period of Support: 03/08/2012 – 02/28/2014
Annual Award excluding indirect costs: $118,614
Disposition: Funded

PI: **Bina Joe**
Agency: NIH/NHLBI
Grant Number: 5-RO1-HL112641-03
Period of Support: 12/01/2011- 11/30/2016
Annual Award excluding indirect costs: $428,645
Disposition: Funded

PI: Harold G. Klemcke
Contractor: **Bina Joe**
Agency: US Army Medical Research and Material Command
Contract Number: W81XWH-12-0052
Period of Support: 12/01/2011 - 01/13/2014
Annual Award excluding indirect costs: $42,724
Disposition: Funded

PI: Michal Schwartzman
Consultant: **Bina Joe**
Agency: NIH/NHLBI
Grant Number: PO1-HL034300
Period of Support: 2011-2016
Disposition: Funded

PI: **Ashok Kumar**
Agency: NIH
Grant Number: R01-HL-092558-06
Period of Support: 02/02/2012 – 06/30/2015
Annual Award excluding indirect costs - $235,620
Disposition: Funded

PI: **Ashok Kumar**
Agency: NIH
Grant Number: R01-HL105113-03
Period of Support: 12/01/2011 – 11/30/2014
Annual Award excluding indirect costs: $245,000
Disposition: Funded

PI: **Beata Lecka-Czernik**
Agency: American Diabetes Association
Grant Number: N-123785-01
Period of Suppport: 07/01/2013-07/14/2016
Annual Award excluding indirect costs: $89,976
Disposition: Funded

PI: Jayasuriya
Co-Investigator: **Beata Lecka-Czernik**
Agency: NIH/NIDCR
Grant Number: R01- DE-023356-01
Period of Support: 07/01/2013-6/30/2018
Annual Award excluding indirect costs: $258,498
Disposition: Funded

PI: **Sonia M. Najjar**
Agency: NIH/NHLBI
Grant Number: R01-HL-112248-03
Period of Support: 01/01/2012 – 12/31/2016
Annual Award excluding indirect costs: $256,805
Disposition: Funded

PI: **Sonia M. Najjar**
Co-Investigator: **Edwin R. Sanchez**
Agency: NIH/NIDDK
Grant Number: R01-DK-054254-12
Period of Support: 03/01/2000 – 04/30/2015
Annual Award excluding indirect costs: $215,033
Disposition: Funded

PI: Amir Askari
Leader of Project 2: **Sonia M. Najjar**
Agency: NIH/NHLBI
Grant Number: 5-P01-HL-036573-25
Period of Support: 04/15/2009 – 03/31/2014
Annual Award excluding indirect costs: $1,077,410
Disposition: Funded

PI: **John W. Turner, Jr.**
Agency: Bureau of Land Management
Grant Number: L10AC20431
Period of Support: 09/30/2010 – 09/29/2015
Annual Award excluding indirect costs: $599,206
Disposition: Funded

PI: **John W. Turner, Jr.**
Agency: Stranahan Foundation
Grant Number: 203397
Period of Support: 07/01/2009 – 06/30/2015
Total Award excluding indirect costs: $31,873
Disposition: Funded

PI: **John W. Turner, Jr.**
Agency: Humane Society of U.S.
Grant Number: N-120280-01
Period of Support: 12/21/2007 – 12/31/2013
Total Award excluding indirect costs: $67,235
Disposition: Funded

PI: **John W. Turner, Jr.**
Co-Investigator**: George T. Cicila**
Agency: PNC, Inc (nonprofit)
Grant Number: 205033
Period of Support: 7/1/2013 – 06/30/2015
Total Award excluding indirect costs: $9,060

PI: **Kathryn Smedlund**
Sponsor: **Guillermo Vazquez**
Agency: American Heart Association (AHA), Great Rivers Affiliate
Grant Number: 12POST11910042
Period of Support: 07/01/2012 – 06/30/2014
Annual Award excluding indirect costs: $44,000
Disposition: Funded

PI: **Guillermo Vazquez**
Agency: NIH/NHBLI
Grant Number: R01-HL-11877-03
Period of Support: 12/15/2011 – 11/30/2015
Annual Award excluding indirect costs: $245,000
Disposition: Funded

PI: Jiang Tian
Co-Investigator: **Zi-Jian Xie**
Agency: NIH/NHBLI
Grant Number: R01-HL-105649-03
Period of Support: 12/15/2011 – 11/30/2016
Annual Award excluding indirect costs: $225,000
Disposition: Funded

Grants Applied for July 1, 2013 – June 30, 2014

PI: **Jennifer W. Hill**
Agency: NIH
Grant Number: 1R01HD081792-01A1
Period of Support: 04/01/2015-3/31/2020
Annual Award excluding indirect costs: $250,000
Disposition: Under Review

PI: **Jennifer W. Hill**
Agency: NIH
Grant Number: 1R01HD081792-01
Period of Support: 07/01/2014-6/30/2019
Annual Award excluding indirect costs: $250,000
Disposition: Not Funded (17%)

PI: **Terry Hinds, Jr.**
Agency: NHLBI
Grant Number: K01 Mentored Career Development Award to Promote Faculty Diversity (RFA-HL-13-019)
Period of Support: 12/01/2014-11/30/2019
Priority score = 20 [payline = 25]
Annual Award excluding indirect costs: $125,175
Disposition: Pending; award anticipated

PI: **Beata Lecka-Czernik**
Agency: NIH/NIA
Grant Number: 2R01 AG028935-06
Disposition: Pending

PI: **Ashok Kumar**
Co-Investigator: **Nitin Puri**
Agency: NIH
Overexpression of Angiotensin Receptor: Inflammation, Oxidative Stress and Aging
Period of Support: 07/01/2013-06/30/2019
Annual Award excluding indirect costs: $450,780
Disposition: Pending

PI: **Ashok Kumar**
Co-Investigator: **Nitin Puri**
Agency: NIH
Period of Support: 04/01/2015-03/31/2020
Annual Award excluding indirect costs: $250,000
Disposition: Pending

PI: **Ashok Kumar**
Co-Investigator: **Nitin Puri**
Agency: NIH
Period of Support: 04/01/2015-03/31/2020
Annual Award excluding indirect costs: $384,533
Disposition: Pending

PI: **Ashok Kumar**
Co-Investigator: **Nitin Puri**
Agency: NIH
Transcriptional regulation of angiotensin receptor by metabolic syndrome
Period of Support: 04/01/2015-03/31/2020
Annual Award excluding indirect costs: $250,000
Disposition: Pending

PI: Marshall University
Co-Investigator: **Nitin Puri**
Agency: NIH
Period of Support: 07/01/2014-06/30/2015
Annual Award excluding indirect costs: $19,454
Disposition: Pending

PI: Griselda Hernandez (SUNY Albany)
Co-I: **Edwin Sanchez** (Consortium)
Agency: NIH/NIGMS
Grant Number: 1R01DK098598-01
Period of Support: 04/01/2015 to 03/31/2019
Annual Award excluding indirect costs: $250,000
Disposition: Pending